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HISTORY OF MEDICAL ETHICS*

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It is impossible for anyone to understand the present situation accurately and look intelligently into the future unless one has the opportunity to acquaint oneself with the sources of knowledge which have reached us. Any state of affairs at the given moment is in reality merely a phase of development and no one knows better than the physician the importance of this law that regards the biologic organization of the individual.

There was a period in the history of medicine when the edifice of medicine was constructed exclusively on Aristotelian logic which was undermined by the advent of experimental science. This universal return to the biologic concept and Hippocratic method shows that medicine cannot be bound to the microscope or the test tube or be confined within the artificial limits of any definite system. The history of the process of evolution in medicine gave us an opportunity to scrutinize the distant origins and structure of our knowledge formed slowly through so many paths to recognize the formation of medical thought by instinct, fear, hope and faith, the result of which gave us the cultural aspect and the basic and directing forces which guide our lives today.

In recent times scientific research and analysis placed in the hands of students gave us many new discoveries which constantly introduced new problems. Modern medicine in theory and in practice is sub-divided into special branches incorporating various techniques and doctrines. Medicine cannot succeed in giving the suffering humanity physical, mental, emotional and social relief unless the high ideals and morality will remain the background of modern medical practice.

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In recent years research has shown that history of medicine should be considered as an accumulation of knowledge and of facts, some of which have been forgotten over centuries and then have come to light again.

The early medical knowledge of the Greeks, which until a few decades ago was regarded by historians as a first expression at medicine, really represents results obtained from the concepts of very early civilization derived from a phenomena occurring in the pre-historic period. The study of the earliest origins of medical thought goes back to the most distant periods of the history of humanity.

In the fourth millennium before Christ there had begun to be formed in the people of Southern Mesopotamia a systematic medical concept from which is derived Assyro-Babylonian medicine.

In the second millennium Egyptian medicine obtained advanced development. At the same epoch the maximum development of Minoan civilization was reached.

A definite medical concept was formed by the people of Israel about 1500 B.C. and the Homeric period began approximately 1000 B.C.

One should remember that the Babylonian medicine was established on the basis of their religious cult and it was above all, magical and empirical, everything dependent upon metaphysical forces.

Many of the present diseases were recognized by ancient Egyptians. In the field of hygiene, Egyptian medicine reached a high degree of progress and one may say there existed a true social medicine in rudimentary form. Daily regulations were enforced for the burial of the dead, there were strict rules for the cleaning of dwellings, for normal diets and sex relations so that the entire daily life of the Egyptian was regulated by precise laws which were closely connected

with the religious regulations controlled by the priests.

The concept of Hebrew medicine is found in the Biblical and Talmudic records where we find that it differs from that of every other ancient people in that they recognize that one God is the source of health and all diseases come as deserved punishment for sins. The idea of malignant demons, magic practices and superstitions were quite prevalent. It is from the one God that the people of Israel demanded the cure of their ills.

The ancient Hebrews established the first codification of hygienic regulation. The art of healing was reserved for the one God. The priests were interpreters and full-fillers of the law and of the will of God, thus the people of Israel did not have professional physicians. The Hebrew hygienic and religious laws permeated the medical ethics and legislation of the Jewish people.

The history of the Persian medicine is divided into two great epochs. The first is that included in the ancient books, Zendavesta, and the other belongs to the Arabian and Mohammedan culture. The ancient Persian medicine flourished in a period where the great empire extended its power from the Mediterranean to the shores of the Indus and from the Caucasus to the Indian Ocean.

A physician who committed wrong in his medical practice was penalized according to the code. Physicians practicing their profession had to pass certain examinations and tests. The Persian ethical concept is much like the Jewish in that they were penalized for wrong-doing and they also had various tests before they could practice medicine.

The medicine of ancient Greece was but one phase of medical thought through the century but this phase of development shows in full strength orientations which in the preceding civilizations were budding germs.

All the knowledge that the different civilizations had contributed to the people in the Hellenic period was collected and utilized for the orientation of their own medical science. In the Hellenic culture freedom of thought, observation and investigation was exercised and through these mediums the development of medicine was guaranteed. We are taught by history, both of the most ancient times and those much nearer to us, that there cannot be any true science without thought, observation and investigation.

In Greece there was never a close priestly caste. Religion was a poetic myth, never a political edifice and it never dominated critical thought. Ideas, therefore could develop freely, contradiction with, and discussions of the most venerable traditions could flourish.

The medicine at the time of Homer was a noble art and he was held in great honor because he was "a man who was worth more than many others." In post-homeric literature we find increased frequency of superstitions, demons, etc. This was through oriental influence. At first all the Gods possessed healing attributes or could cause disease but later particular powers were attributed to only a few among them. The inventor of the healing art was Apollo "who chases away all ills." The Centauer "Chiron" was generally regarded as the founder and master of medicine, particularly surgery. The famous Greek heroes were his pupils in the healing art. Ascalapios, in Latin, Aesculapius, the pupil of Chiron, became in Greecian mythology, the son of Apollo and the God of medicine. Aesculapius is represented always by the serpent, the symbol of the God and his healing power. The cult of Aesculapius was introduced about 429 B. C. The more recent historical investigations showed that if Homeric medicine was practised by laity; the medical sanctuary of Aesculapius was practised by priests and the cures were regarded as miraculous.

It was the great philosophic school to which Aristotle gave the name Italic that became the most important basis of scientific medicine. If it reflected Ionic influence it was because Pythagoras, its founder, was of Ionic origin. Before Pythagoras arrived at Croton, there was an important school of medicine and it was near this school that Pythagorism had its development. We note that Pythagoras was a physician penetrating and deep observer of animal organisms particularly curious about the phenomenon of procreation. Pythagoras's philosophy had an understanding for Hippocratic medicine and the healing powers of nature. According to Pythagoras's theories, health consists of a state of perfect

harmony. The disease is nothing but an expression of disturbance of such harmony. Cure consists of return to this harmonious state.

Thus the soil for the Golden Age of Greek medicine, the Hippocratic medicine, was prepared. Hippocrates the physician and master dominated the schools and physicians of his time. He stands above priestly medicine as he does above empirical medicine and includes in his person, idealized throughout the centuries, the sum of the knowledge of the past. Hippocrates, according to Soranus' writings, was born in 459 B. C. on the small island of Cos. He died in 355 B. C. at the advanced age of one hundred and four. He was regarded as the father of medicine. He was the best known physician of his time and the most profound investigator and acute observer. He established the facts that disease was a natural process, that symptoms were reactions of the body to disease and the function of the physician was to aid the natural forces of the body. He taught that the physician should be a gentleman, a man of honor, and he established his famous oath which has endured through the ages as a shining ideal.

"I swear by Apollo the physician, and Aesculapius, and Hygeia, and Panacea, and all the gods and goddesses, that, according to my ability and judgment, I will keep this Oath and this stipulation—to reckon him who taught me this art equally dear to me as my parents, to share my substance with him and relieve his necessities if required; to look upon his offspring in the same footing as my own brothers, and to teach them this art, if they shall wish to learn it, without fee or stipulation, and that by precept, lecture, and every other modes of instruction, I will impart a knowledge of the art to my own sons, and those of my teachers, and to disciples bound by a stipulation and oath according to the law of medicine, but to none others. I will follow that system of regimen which, according to my ability and judgment, I consider for the benefit of my patients, and abstain from whatever is deleterious and mischievous. I will give no deadly medicine to anyone if asked, nor suggest any such counsel; and in like manner I will not give to a woman a pessary to produce abortion. With purity and holiness I will pass my life and practice my art. I will not cut persons labouring under the stone but will leave this to be done by men who are practitioners of this work. Into whatever houses I enter, I will go into them for the benefit of the sick, and will abstain from every voluntary act of mischief and corruption; and, further, from the seduction of females or males, of free-men and slaves. Whatever, in connection with my professional practices, or not in connection with it, I see or hear, in the life of men, which ought not to be spoken of abroad, I will not divulge, as reckoning that all such should be kept secret. While I continue to keep this Oath unviolated, may it be granted to me to enjoy life and the practice of the art, respected by all men, in all times. But should I trespass and violate this Oath, may the reverse be my lot."

This oath shows to what ethical heights the concept of medical practice had reached even in the early medical schools of Greece.

Roman medicine was much influenced by the Greek and reliable physicians were mostly Greeks.

Celsus was the most powerful and intelligent mind in the medical history of classical Italy. He was a worthy disciple of Hippocrates in the field of medical ethics. He recognized and loudly proclaimed that physicians should admit their errors believing that "the simple error committed is proper for a man of great intelligence because thus he may be useful to those who follow and prevent others to be mistaken as he was mistaken."

The historians are still in a quandry whether the Roman medicine had a decisive effect on the progress of medical sciences or whether the Greek medicine gave the necessary push to the whole Roman civilization. Many historians believe that what Romans did and knew in the domain of medicine was not entirely without the effect of Greek teaching and Greek initiative. However, the Romans deserve credit in medical history for many achievements. It was only in Rome that the physicians constituted a class protected by law for which the state accorded special guarantees. In fact, it was the Roman genius who snatched physicians from uncertain positions and guaranteed him the rights of citizenship

and placed in his hands the supreme responsibility for public health.

The Christian era exercised a determined influence on the development of medicine. It gave a different evaluation of human life; a fraternal concept of equality and charity which imposed on all the faithful the most severe sacrifices in order to lessen suffering of others. The renewal of religious fervor on the one hand, and the influence of oriental currents on the other, developed along with the purely religious medicine a popular medicine which followed ancient concepts in its recourse to the cult of the saints.

The first Christian physicians practiced medicine by preaching the all importance of faith and recognized the complete authority of the Nazarene, whose Gospel is addressed to suffering humanity awaiting salvation.

Under the influence and domination of Christianity medicine became dogmatic, of which faith was the first article. Its essential aim was the assistance of the sick regarded as a work of human and divine pity.

At the same time the flourishing period of Arabian medicine was progressing its work throughout the Asia Minor. Christianity in its rapid spread, changed its direction of the study of literature and art but at the same time had preserved the achievements of the ancients.

In later centuries following the tradition of the Orient and Greecian institutions, the hospitals were built around the monasteries. In these times of bloody conflict no one could find the peace and calm necessary for the sick outside of the religious orders which had been able to acquire the respect of men of all factions. It is thus that a monastic medicine arose which later flourished thanks to such orders as the Knights of Saint John, etc. Montecassino acquired great fame throughout the West and the teaching of medicine was spread by the Benedictines to the monasteries scattered over Europe.

The chronicle of the early centuries of the middle ages demonstrated incontestably that even in the most depressing times medical thought continued its advance, no matter how slowly, and lay medicine exhibited an uninterrupted historical continuity. And so the memorable School of Salerno was established whose name has remained famous throughout the centuries. This School reached its greatest splendor in the 12th century and preserved its fame to the end of the 14th century. Thus the medical School of Salerno played an important role in the development of a lay medicine and these ideas spread throughout Western Europe. The currents from Salerno activated the French School at Montpellier. And so gradually throughout the European continent there were laws prohibiting from the practice of medicine, anyone who had not shown in his state that he had finished the necessary course of study. Gradually the various states promulgated strict laws for the study and practice of medicine. After a preliminary three years course the prospective physician had to take a five year medical course followed by a year as an experienced practitioner and then he had to pass a formal examination and present a testimonial satisfactory to the authorities.

Thus we find well-organized medical schools at the end of the 15th century and lawns governing the practice of medicine with severe penalties for those who practiced without the necessary license. Strict ethical rules were observed. A fine was inflicted on any physician who spoke evil of another in public. The practice of medicine was entirely in the hands of the laity. It is at this time that we saw a body of professional laws so adequate and well thought out that even up to our present time it has not been necessary to make any considerable changes.

It is worthy of mentioning that the medical physician usually did not care to practice surgery which was regarded as an inferior art and unworthy of scholars. However, the physician often gave written surgical advice but abstained from all practice of surgery which was left to the surgeons proper and to the barbers. The surgeon at the period did not possess university rank. In England the barbers began as a religious guild but later they joined the surgeons with a charter granted to them by Henry VIII. The union of barbers and surgeons lasted until 1745. After the dissolution of the Surgeon Company, the present Royal College of Surgeons was founded in 1800.

Medicine progressed in various countries

throughout the world in conjunction with other sciences. It progressed in France under the leadership of Laennec (1781-1826), Pasteur (1822-1895), Charcot (1825-1895) and others. In Germany, under Paracelsus (1493-1541), Haller (1708-1777), Virchow (1821-1902) etc. In England, under Sydenham (1624-1689), Thomas Percival (1740-1804) who published Medical Ethics in 1803, Lister (1827-1880) who lived with the Hippocratic ideals and Mott (1853-1926). In Russia, under Metchnikoff (1845-1916) who contributed so much to medical ethics. And in the United States and Canada the great physicians and surgeons practiced what they preached in ethics. Osler said that the doctor should be truthful, temperate, charitable, discreet, and cautious. Franklin H. Martin drafted the fellowship oath of the American College of Surgeons and did much to put that organization on its high plane of medical ethics and standards. Wagenstein deplored the low character of those who perform unnecessary operations for gain.

In 1873 the American Medical Association organized its Judicial Council to deal with matters of medical ethics. The principles of medical ethics of June 4, 1912, a revision of the 1847 code, may best be summed up by saying that they are an expression of the Golden Rule.

Non-legal ethical matters are considered by various councils of medical societies. Purely legal ones are taken care of by the courts. Naturally the public is the supreme court as far as individual medical practice is concerned.

A young physician's drive should be love of his work with the acquisition of money a secondary consideration. "He cannot be a real physician unless he chooses the profession for the good he can do rather than the goods he can acquire". (Dr. Anderson). A worthwhile physician never ceases to be a student. The future of every physician's career depends on his professional ability and his character. The latter reflects itself in the manner in which the physician gets along with his colleagues and the consideration which he shows his patients. It is true that we have in the course of time built a sentimental and romantic history of our profession in which most physicians believe. We assume that the physician was at all times the wise and worthy gentleman, highly respected in his community sacrificing himself disinterestingly for the benefit of his patients. In order to satisfy our romantic desire for an ancestor and a symbol we have almost defied Hippocrates. Yet in expressing the ideals in our oath we create in ourselves, particularly in our early practice, a severe conflict because many of the promises which we make in our oath, sooner or later are broken.

In various stages of the development of the medical profession, new and more realistic factors have been incorporated in individual physician's inner thinking mechanism. Every society requests of its physician that he have knowledge, skill and devotion to his patients and a strong morality to withstand various temptations with which he is confronted. The changes are determined primarily by the social and economic structure of society and by technical and scientific means available to medicine at the time.

Many blistering attacks have been made on the medical profession because of individual or group professional ignorance and incompetence, thus encouraging people to make the rounds of doctors and even cultists and quacks.

Dr. Norman F. Miller of the University of Michigan Medical School investigated "246 hysterectomies performed in 1945 in ten different hospitals located in large and small communities. In each case the removal of the uterus was subject to careful pathological examination. The results showed that 76, or almost one third of the entire series, did not show any evidence of the disease." Dr. Miller concludes that "hysterectomy in the absence of pelvic disease cannot be justified any more than the removal of any normal organ."

It is the duty of the medical practitioner to place the interest of his patient above all other considerations and to do his utmost to promote his patients' welfare. Everyone engaged in active practice whether general practitioner or specialist is liable, in his daily work, to false charges, sometimes serious for professional negligence or incapacity. He is always at the mercy of any person who may

feel aggrieved. The majority of allegations of negligence are set up as a counter-claim against the payment of professional fees. The mere employment of a medical practitioner does not imply a contract to perform a cure, but only that the medical practitioner will exercise reasonable care and skill having regard for his position in the profession.

A distinction is drawn between the art and the science of medicine. The art in its Hippocratic sense has reference, among other things, to the practicing doctor's ability to inspire confidence in his patients and in their relatives. This requires on his part an understanding of human nature, abounding unselfishness and observance of the Golden Rule. It calls for the exercise of common sense in the handling of many domestic problems, not always relating to ill health, which so often makes him an indispensable person in those households that have learned to accept him as confidante or advisor. Medical ethics seen at its real light may be looked upon as the prescribed course of morals and manners for the medical man. It is the eternal glory of the medical profession that its code of morals is so strict as to be called "particular."

The relation of the physician to his patients, to one another and to the public, have formed the theme of many discourses and they are well set forth in the principle of medical ethics adopted by the American Medical Association in 1903. Some physicians instinctively follow these rules without perhaps ever having seen them. Others seem never to understand them even after hard study. How unfortunate is the man who cannot live up to the principles of medical ethics! The study of medicine does not bestow on a man more brains or better reasoning power. According to the measure of his individual capacity, his reasoning power is trained and he is furnished with more tools for his mind to use. How does he employ them—that is the test.

Various promises based on idealistic philosophy and ethical exhortations are mostly emotional self deceptions.

It is very unfortunate that we do not submit ourselves to a thorough examination; many of us would at times have failed to pass. Rigid self-inspection is the surest way of keeping sound in medicine and it is but to our advantage to overhaul ourselves now and then and find out what we really are.

The doctor should never forget to perform his civic functions at a high level. Every member of the medical profession should strive every day to make himself a better doctor and it is his duty to be interested in everything that will help to improve his community.

The future of a free medical profession will depend not on glorified, exalted sentiments of the past but upon true understanding of each individual practicing physician of his obligation to medical science, to his patients, to the public and to humanity as a whole. This individual understanding will create a group of realistic performances of duties by the members of county and state medical societies under the guidance of our great national organization, the American Medical Association and thus we will continue to remain a united national force, which will remain vigilant to the ideals of a free profession. No government will ever be able to exercise and influence the people to vote for any socialized or federalized medicine without changing the political and social structure of our country.

Proudly we claim to be members of the second oldest Medical Society in the United States. Let us unite and uphold the principles of high medical ethics in the practice of our profession as our forefathers did. Let us take more positive steps to guard our medical ethics and be courageous in ousting from the society those who do not adhere to the principles of our great society.

Let me close my address with the prayer, in part, from Maimonides (1200) who harmonized biblical and rabbinic teaching with the philosophy of Aristotle.

THE PRAYER OF MAIMONIDES (in part)
1135-1204 A. D.

Almighty God! With infinite wisdom has Thou shaped the body of man. Ten thousand times ten thousand organs has Thou put within it that move in harmony and without ceasing to keep in all its beauty the whole, the body, the envelope of the immortal soul . . . .

To man hast Thou given the wisdom to soothe his brother's sufferings, to know his disorders, to extract what substances may

heal, to learn their powers, and prepare and use them suitably for every ill . . . .

Inspire in me a love for my Art and for Thy creatures. Let no thirst for profit or seeking for renown or admiration take away from my calling . . . Keep within me strength of body and of soul, ever ready, with cheerfulness, to help and succour rich and poor, good and bad, enemy as well as friend. In the sufferer let me see only the human being.

If those should wish to improve and instruct me who are wiser than I, let my soul gladly follow their guidance; for vast is the scope of our Art.

In all things let me be content, in all but the great Science of my calling. Let the thought never arise that I have attained to enough knowledge, but vouchsafe to me ever the strength, the leisure and the eagerness to add to what I know. For Art is great, and the mind of man ever growing.

Almighty God! In Thy mercy Thou hast chosen me to watch beside life and death in Thy creatures. I now go to the work of my calling. In its high duties sustain me, so that it may bring benefit to mankind, for nothing, not even the least can flourish without Thy help.

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MANAGEMENT OF ACUTE CARDIAC INFARCTION

With Emphasis on Recent Trends*

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Statistical analysis of causes of death cannot fail to impress us all with the importance of cardiac infarction. In 1942, nearly 400,000 persons in the United States died of heart disease[1] and a little more than one-fourth of this number (113,636)[2] died of diseases of the coronary arteries and angina pectoris. This figure represents 8.5 per cent of all deaths. Approximately 30 per cent of all patients suffering from heart disease have coronary artery involvement. The death rate from attacks of acute coronary occlusion has been estimated at about 20 per cent, which means that the incidence of attacks of acute coronary occlusion is about 600,000 to 800,000 per year in the United States. (Fig. 1)

Four conditions have been put forward as being reasons for a considerable increase in the number of cases of coronary occlusion: (1) lengthened span of life, (2) ageing of the population, (3) improved diagnosis and treatment of the disease, and (4) greater accuracy in terminology.

According to its mode of onset, one may classify two types of cardiac infarction: (1) the slow onset, and (2) the sudden onset. The slow onset is heralded by the occurrence of precordial pain on exertion or excitement and such symptoms may precede actual occlusion by weeks or even years. Treatment of this type begins with measures to prevent or delay the actual occlusion. Such measures are important in that, by the slow closure of the coronary vessel, the potentially infarcted area is given time for its collateral circulation to develop, thereby making the area of infarction smaller or perhaps avoiding infarction altogether. These measures include (1) the avoidance of things which overload an already constricted coronary, such as physical strain, overeating, nervous excitement, and infection, and (2) the avoidance of things which further constrict the already narrowed coronary, such as smoking, severe chilling, and again, nervous excitement. These things perhaps need some discussion for clarification. For example, the patient with moderate coronary narrowing may actually cause some dilation of collateral vessels by exertion. We have seen many examples of this, one of which was in a man of 60 years who, on chopping ice in front of his garage, could work only about one minute before the onset of chest discomfort. He would then rest until the pain had disappeared, and when he resumed chopping ice, he could work for three to five minutes before the return of pain. I have seen this

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repeatedly described by patients on walking. At first they could walk only a short distance; then after resting they could walk twice or three times as far at the same speed before the return of pain. But the patient should be warned that he must not continue the exertion when the pain occurs. To do so runs the risk of incurring immediate infarction.

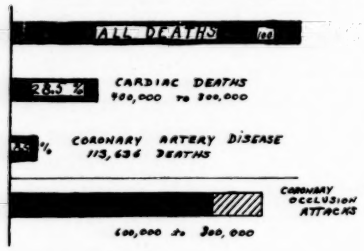

FIG 1 STATISTICAL RELATIONSHIP OF CARDIAC DEATHS AND DEATHS DUE TO CORONARY DISEASE TO DEATHS FROM ALL CAUSES. A SEPARATE COLUMN PORTRAYING THE NUMBER OF CORONARY OCCLUSION ATTACKS IS SHOWN.

Exertion soon after eating throws a double load on the coronary circulation. Advice to this type of patient, therefore, should be to avoid exertion until a full meal is well on its way in the digestive tract. As mentioned before, moderate exertion, just short of producing pain, may be a therapeutic aid by causing increased collateral circulation. We therefore encourage exertion to the point just short of pain in these patients, always warning them to stop upon onset of pain until it has disappeared.

Nervous excitement may both increase the work thrown upon an already narrowed coronary circulation and also further constrict it. The constriction may be worse than the dilatation of increased work, and we therefore warn against all nervous excitement.

Infection obviously creates a tremendous load upon all circulation, and such a load is not subject to the control that the load of effort is. Moreover, the toxic effect of the infection may have a deleterious effect upon the vessels as well as the heart muscle itself. The patient should be warned carefully to avoid exposure to all kinds of infection, and to place himself under immediate and thorough treatment to rid himself of even minor infections as soon as they become evident.

Smoking can be shown to constrict blood vessels all over the body. Perhaps, in one accustomed to smoking, this effect may be less; but certainly a degree of constriction occurs in everyone even on one cigarette. In one patient who had smoked cigarettes all his adult life, at the age of forty-six years the onset of a coronary occlusion was first initiated upon smoking a cigarette. He promptly desisted, and upon trying to smoke again a few minutes later, the pain promptly returned. Patients who suffer from angina often complain of more frequent attacks when they smoke. Scientific support for this effect of smoking on blood vessels can be had by the observation of a drop in skin temperature as recorded by a thermocouple upon smoking just one or two cigarettes.[3]

Severe chilling is frequently associated with the onset of acute cardiac infarction, especially if it is combined with exertion. Several times I have known infarction to occur when the patient drank a very cold drink when overheated. Also, jumping into cold water or taking a cold shower is a commonly associated event. I have grown to fear the exertion of shoveling snow in a patient who has had any symptoms suggestive of cardiac involvement. It combines severe activity, to which the patient is usually unaccustomed, with hurry and cold.

Examples of anginal pain and cardiac infarction precipitated by nervous excitement are so numerous as to make the necessity for avoidance of it self-evident. Cardiac catastrophies following automobile accidents, deaths of other members in the family, and many other events of nervous stress, are common-front-page news.

Drugs which have a helpful action in improving coronary collateral circulation, thereby delaying infarction, include the nitrites, the theobromines, and certain other miscellaneous ones.

Nitroglycerin, gr. 1/100 in a hypodermic tablet, placed under the tongue at the first evidence of pain, or preceding some necessary effort which has produced pain before, will help many patients to carry on with ordinary activity. Other more slowly acting nitrites have virtue in the presence of hypertension in many instances. This treatment cannot be depended upon to keep blood pres-

sure down, however. The use of potassium thiocyanate, gr. iii (Gm. 0.2) twice daily, in patients with hypertension may reduce the frequency and severity of anginal pain and the coronary constriction associated. Thiocyanates should be used with great caution in patients with impaired kidney function even in the above dosage; and in dosage higher than that, in every patient, laboratory control of blood levels—not to exceed 12 mg. per cent—should be insisted upon at regular intervals. The theobromines, such as theobromine calcium acetate, calpurate, or purital, in the dosage of 7½ grains (Gm. 0.5) four times daily may diminish attacks. Aminophyllin in the conventional dosage of gr. 1½ (Gm. 0.1) four times daily is without much if any effect when given by mouth. However, dosages of gr. iii to gr. vi (Gm. 0.2 to Gm. 0.4) four times daily may be effective. In this dosage it may nauseate the patient unless it is given in enteric-coated tablets. Suppositories of aminophyllin, gr. vi (Gm. 0.4) may exert some effect in reducing anginal pain and may be used several times daily. Mild sedation such as phenobarbital, gr. ¼ (mg. 15) three or four times daily, may be helpful.

When the patient reaches the stage of actual closure of the vessel, the above suggestions may make the closure so gradual that the infarction is minimal; and the patient's reaction may be attended by little or no pain and no shock. In any case, whether or not the patient has had any previous warning, and especially if the pain is severe and if there is any evidence of shock, the very first indication is to relieve the pain as quickly as possible. This can best be done by the hypodermic administration of one of the hypodermic narcotic preparations, such as morphine sulphate, gr. ¼ (15 mg.), dilaudid, gr. 1/20 (mg. 3), pantopon, gr. 1/3 (mg. 20), or demerol (50 to 100 mg.). Usually these preparations are best administered hypodermically and followed by a waiting period of at least 20 minutes before a second dose is given. Some authorities believe the first dose should be given intravenously to shorten this waiting period. This avenue of administration is quite safe if the patient's reaction to morphine is previously known. It is occasionally attended with quite severe vomiting, which in part defeats the purpose of its administration. Some caution is necessary in the severely shocked patient or severely dyspneic patient to avoid the overdosage of any sedative which may depress the respiratory center, the efficient action of which may be 100 per cent necessary to maintain life. Many times have I thought that injudicious enthusiasm to relieve the patient's pain in a hurry, perhaps under pressure of an anxious family, has been the determining point in the patient's demise. Narcotics are, of course, strong depressants of the respiratory center; but one should also remember that even barbiturates in full dosage may be respiratory depressants. Nevertheless, the relief of the pain is the most important aim in the early treatment of the shock state and some risk must be taken.

From the onset of the pain the patient should be placed at rest. The term "rest" may be a relative thing during the agitated stage. Certainly the patient should never be forcibly restricted. To do so will only increase his effort, and he may thereby be deprived of the opportunity to assume some fairly comfortable position. He should be placed in as comfortable position as possible and encouraged to avoid agitation. If the accomplishment of this aim necessitates transportation to another room, or up a stairway, or even to a hospital, it should be done with the least possible effort. The best time for this movement is after the patient's initial pain or shock can be relieved. It is better to move the patient in the first two days than later when the infarcted area has reached its softest stage. I have allowed a patient to move up a stairway by his own effort, after the initial pain was over and there was insufficient help to carry him, by having him sit on the lower steps and in the sitting position raise himself one step at a time, resting on each one, until he has reached the top. The state of the patient's heart action and circulation at the time must determine the wisdom of such action. Then the question will arise, particularly in older patients, as to whether or not he should be allowed to go to the toilet. Again, much individual judgment is necessary in each case; but if it entails more effort and strain on the part of the patient to drape himself over a bedpan than to sit out on a com-

mode or pan placed on a chair, then my vote is for the bedside commode, and this from the first day onward. Obviously, the severely ill patient cannot do this; but some loosening of the old restriction of having the patient lie rigidly in bed without motion for six to ten weeks is outmoded as a routine thing. We will refer to this point again when we discuss rehabilitation.

In the patient who is severely shocked, the problem of circulatory collapse brings up the question of intravenous administration of fluids. The possibility of overloading the circulation is always present; but by carefully limiting the amount administered in a given time and observing the result before further quantities are given, one should prevent catastrophe. The selection of the solution to be given may depend upon the condition of the patient. If shock is the predominant difficulty, whole blood or plasma in 250 cc units should be tried first. Later, 5 per cent glucose in distilled water or saline may be given if the patient is unable to take food by mouth, always taking care not to give too much salt by vein. In this connection, it is well to alternate the 5 per cent glucose in saline with 5 per cent glucose in distilled water in 1000 cc amounts and give fairly slowly with a rest interval between bottles.

Feeding by mouth should be started as soon as the patient is capable of taking food and continued in small amounts at three-hour intervals until he is able to take larger quantities. The importance of keeping up nutrition, particularly of protein foods, has become much more evident to us in our patients in the Pennsylvania Hospital since Duncan's work showing the frequent inadequacy of food intake in long-term illnesses.[4] Attention to the food intake has, we believe, significantly improved the recovery rate of our patients suffering from infarction as well as from other protracted disease.

The administration of drugs in the acute shock stage attempts not only to relieve pain but also to improve collateral circulation in the infarcted area, to stimulate the respiratory center, and to stimulate or support the heart muscle itself.

Firstly, in the acute stage, aminophylline, gr. 3-¾ (Gm. 0.25) intravenously, may produce remarkable effect in relieving dyspnea and supporting cardiac action. It should be injected slowly over a three-minute period and may be repeated as frequently as every half-hour for several doses.

Coramine may be given similarly but is usually given in insufficient dosage. Three or four ampules are usually necessary to produce demonstrable effect.

As mentioned for prevention, the theobromines, such as theosodate, calpurate, purital, or other, may be given by mouth as the patient is able to tolerate them; but medication should not be given by mouth at the expense of omitting food because of nausea produced by the medication.

Papaverin in 2 or 3 grain doses four times daily may be given for its effect in improving collateral circulation. It has little effect in relieving pain in the acute stage even though it is a narcotic derivative.

Nicotinic acid up to 100 mg. four times daily also helps in improving collateral circulation.

Quinidine may be necessary in the prevention and control of cardiac arrhythmias and tachycardias which occur not infrequently in association with acute infarction. It may be given in doses of gr. iii (Gm. 0.2) to gr. vi (Gm. 0.4) every six hours.

The anticoagulant, dicoumarol, in an extensive study involving 1000 patients with infarction and using 1000 patients with infarction as controls, has been shown by Wright and his co-workers to reduce the incidence of complications due to thromboses as much as 15 to 20 per cent.[5] This is a significant figure, since it is known that in all cases as many as 7 to 8 per cent die of such complications.[6]

The administration of dicoumarol is not without some danger; but as Wright has shown, the difficulties encountered are unimportant as compared to its benefits. Nevertheless, due precautions should be taken to prevent trouble. It prolongs coagulation time by depression of the prothrombin level through its action on the liver. *Daily* prothrombin levels should be determined by a competent laboratory and control levels should be run with every batch of the thromboplastin used in the determination. The effect of a single dose is not evident for about forty-eight

hours. This delayed action of the dicoumarol and its variable effect in different patients makes the dosage very difficult to estimate. (Fig. 2) shows the difficulties encountered in one case, which is not unusual. In some individuals in the early stage following infarction the prothrombin time is increased even before dicoumarol therapy. We have therefore avoided the use of heparin except in cases in whom some thrombotic lesion was already present before dicoumarol was started. The forty-eight hour delay is not deleterious in most cases. The dosage of dicoumarol should be judged to keep the prothrombin level between thirty and fifty seconds. However, unless some untoward symptom occurs, such as nosebleed, bleeding gums, or subcutaneous bleeding, one need not be disturbed by higher prothrombin levels more than to discontinue the dicoumarol until the prothrombin level drops to the desired figures. Dosages may vary considerably in different patients. Wright recommends an initial dosage of 300 mg. followed by 100 to 200 mg. daily afterward, according to the prothrombin levels obtained. In our experience doses somewhat lower than this have been effective, viz., 200 mg. initial dose and 100 mg. daily following. The maintenance dose may change from week to week as treatment continues. No letup in watchfulness in determining prothrombin levels therefore can be considered safe. Dicoumarol is continued until the patient is regularly getting out of bed for a good part of each day. This period requiring dicoumarol is usually from three to four weeks—longer in severe cases.

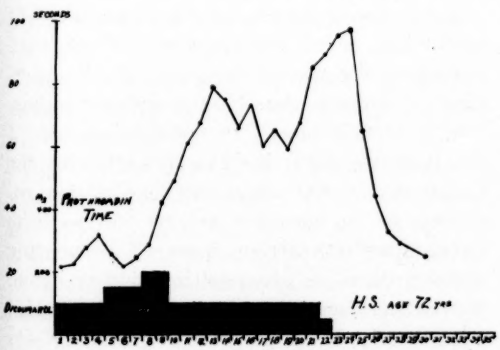

FIG. 2 SHOWING PROTHROMBIN RESPONSE TO DICOUMAROL DOSAGE

When complications referable to the heart itself occur in the presence of cardiac infarction, they should be treated in the same manner as the condition would be treated without infarction. If cardiac failure occurs, digitalization should be carried out promptly and in the same manner as if infarction were not present. Withholding digitalis because of the possible excessive strain thrown upon the softened infarcted area is not justified. Oxygen therapy may be helpful. Other medication in emergency, such as intravenous aminophylline, coramine, and caffeine may be necessary.

Should some other complication occur, requiring surgical interference, the dicoumarol should be discontinued and the surgery delayed until the prothrombin level is again normal or nearly so. If the surgical procedure must be hurried, then transfusion may reduce the prothrombin level more rapidly. The administration of large doses of vitamin K intramuscularly or intravenously may also hurry the drop of the prothrombin level to normal. In shocked or severely ill patients, the use of penicillin may be justified to prevent hypostatic pneumonia.

The problem of mobilization of the patient was mentioned previously. It is my practice, if the patient's condition allows it, to permit the patient to use a commode beside the bed as soon as he has recovered from the initial shock. Otherwise, he remains in bed until the sedimentation rate, taken once each week, shows a definite drop toward the normal; and finally when the sedimentation rate has reached normal, activity is gradually increased, allowing him to sit out in a chair for increasing periods of time until complete mobilization is attained at the end of six or eight weeks. At this time, re-evaluation by electrocardiogram and chest film will aid the summary of the clinical picture in deciding when the patient may resume his work and how much of the original job he may be able to do.

SUMMARY

1. The statistical importance of cardiac infarction is emphasized.
2. Two types of treatment of cardiac infarction are described: (a) for slow onset, and (b) for sudden onset. Preven-

tative measures are outlined in some detail.

3. Treatment of the patient after infarction is discussed, including (a) therapy of shock, (b) consideration of rest, (c) use of drugs, and (d) management of complications and their prevention by dicoumarol therapy, mobilization, and penicillin.
4. A short discussion of rehabilitation is given.

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DISCUSSION

DR. E. R. MILLER (Wilmington): I am sure we have all enjoyed this comprehensive review of modern treatment of myocardial infarction, which is commonly known as the physician's disease, as this year in our Society there were six deaths, and 50 per cent of these were from myocardial infarction. In other words, it is a disease that lies close to the hearts of all of us, and Dr. Carey certainly has reviewed very nicely the subject in general.

However, I think the physician who is particularly interested in cardiology, taking all the known facts of this treatment, thinks along the line, "When *we* get our coronaries, how would we like to be treated, particularly with reference to the modern treatment with dicumarol and heparin? Would we like to have them or wouldn't we?"

There is no question that Colonel Wright reported 1000 cases, which, of course, was work done by the American Heart Association throughout the country, where one case would be admitted to the hospital and not receive dicumarol, and the following case would. He was given the privilege of reporting all these cases from the large medical centers, and I am sure that his statistics sell themselves in the fact that dicumarol is definitely indicated. However, there are many problems that arise with regard not only to dicumarol but also to heparin.

A recent review of the Mayo Clinic, which to me is much more in detail than Colonel Wright's work, by Parker and Barker, of 50 cases is quite convincing. They reported 100 cases on which they used dicumarol, some of them with heparin and some not with heparin, and they compared them to 100 cases that May and Barnes had reported three years before, in which dicumarol and heparin were not used. That was in 1945.

When dicumarol was not used, there were 37 per cent of these 100 cases that had vascular complications, while in the Parker and Barker cases of 100, they used dicumarol and, as I said, in some cases used heparin in conjunction with it, with only 5 per cent vascular complications. Just think of the 37 per cent as compared to 5 per cent.

Then, with respect to secondary myocardial infarction in the series of 100 without, 15 per cent had secondary myocardial infarction while only 2 per cent of those with dicumarol had it.

Pulmonary embolism, 14 per cent without, and only 1 per cent with.

Thrombophlebitis, 7 per cent without dicumarol, and no cases of thrombophlebitis where dicumarol was used.

Arterial occlusion, 4 per cent without dicumarol, and not one case with dicumarol.

Certainly these are convincing reports, but don't be misled that with it the mortality was reduced so much, because in May and Barnes' cases of 100, the rate of mortality was 13 deaths in 100, while with dicumarol, Parker and Barker's cases, 11 deaths.

So therefore, as the speaker stated, the mortality is definitely reduced, but it is not reduced in proportion.

There are a couple of questions which I would like to ask the speaker. First, with regard to the use of heparin. As I understand it, heparin does have a definite indication in certain cases. In my own practice, I use it definitely if the case is early, for the simple reason that where you have arterial occlusion in the coronary artery, you want to have immediate action there of preventing either a distal or proximal invasion or extension of the thrombus. If the heparin is used immediately, it can perform this function, As I see it, that is about the only use and indication for heparin.

However, if you get a case later, anywhere, we will say, from four days on—because the complications of coronary thrombosis, myocardial infarction, occur as shown by the statistics anywhere from four days to 20 days, most of them, and then dicumarol alone can perform its function of preventing these complications which I have mentioned, namely, vascular complications and pulmonary embolism, coronary thrombus, and arterial occlusion.

I understood the speaker to say that he did not use heparin so much, and I would like to ask him if that is a definite rule with him, because I feel that heparin, as I have said, is indicated where you get a case early.

Dicumarol itself certainly is not a toy and, unfortunately, has to be used in the hospital, but certainly with such a disease as myocardial infarction, it is just as important to move a case to the hospital as a case of appendicitis, when we know honestly that many cases of appendicitis would subside but we are not going to take any chances. We do not have a right to take a chance with such a serious illness as myocardial infarction.

So, as we say, the drug has to be carefully watched, but certainly these two anticoagulent treatments have been great advances in the treatment of myocardial infarction and it remains for us, as physicians, to become more acquainted with them and to use them wisely, adequately, early enough, and in the proper place.

Again, I want to thank Dr. Carey, and I would like to ask him another question, about Pitkin's solution as a medium for heparin, whether there is any advantage with that as compared to the use of plain heparin intravenously.

Another question is how long he uses dicumarol in his cases, how long does he keep up the medication.

DR. J. R. DURHAM, JR. (Wilmington): I want to thank Dr. Carey very much for a good paper.

I have one question in mind, and that is whether dicumarol has any effect on the sedimentation rate, or, rather, what degree of effect it has.

Sometimes we are hard put to know how soon to get these patients out of bed, and we do know that the sedimentation test is a nonspecific test, influenced by other factors in the body than perhaps a single inflammatory focus in the myocardium. Occasionally we see cases which seem to respond clinically and by electrocardiogram, who run a rapid sedimentation rate, and at times we are inclined to blame it on the dicumarol.

The other point I have in mind is that in our cases, when we get them early, we have been using dicumarol only, since it has been shown in animals that the dicumarolization will prevent the mural thrombus.

It is my understanding that in this early period of infarction we have a period of grace of three or four days before the muralthrombus forms, and I would like to hear Dr. Carey's points on that.

DR. CAREY: In replying to the questions presented, I should say that there are a number of these questions which would get different personal reactions in any group. Some are not subject to scientific investigation, and, of course, are bound to be matters of opinion. The question as to the time to allow the patient out of bed following an infarction is an illustration. I will come to that in a minute.

First, as to Dr. Miller's discussion of cardiac infarction being a physician's disease, there has been a fairly recent statistical study by Master, published in the *American Heart Journal*, in which he says, after a careful analysis of causes of deaths among physicians as well as other groups, that infarction is not more frequent among physicians than it is among any other group of persons who live a comparable life. As physicians, therefore, we cannot feel that we have any "corner" on this disease.

Dr. Miller also mentioned the question of "heparin," and I think it must be considered. I did not mention it in my paper because we do not use it routinely. We have no objection to using it, except in the occasional patient who will be shown to have a rather high prothrombin time at the outset. However, heparin is thought to be unnecessary since mural thrombi perhaps do not get very much chance to form before dicumarol action starts if one is able to see the patient early after infarction occurs. I believe Wright and his coworkers have adopted this plan also. Obvious-

ly, if the patient has evidence of some thrombosis, or some condition which potentially suggests it, he should have heparin immediately. As to the Pitkin menstruum of heparin, I think it can be used quite successfully and see no objection to it. If one has the patient under conditions of rather close control, however, the Pitkin menstruum is really not necessary, because heparin can be given intravenously with an ordinary hypodermic syringe and needle in the dosage of 50 mg. every six hours. In hospital practice, therefore, it becomes less necessary to use the Pitkin menstruum, and the expense being a factor, we do not use it.

The question as to how long dicoumarol shall be continued is also an arguable point. Wright, I believe, says that they continue it for about four weeks rather arbitrarily. In our practice, we have used it for the length of time that the patient remains in bed, and when he starts being mobilized and is up and around for a fair amount of time, we then discontinue it—usually in three to four weeks.

Dr. Durham asked about dicoumarol and its effect on sedimentation. I have discussed this point with some of our laboratory men and they tell me that perhaps it does have a slight effect on the sedimentation rate, but not very much, so that practically we disregard it. I would like to hear Dr. Howard's opinion on that.

The question of how soon to get the patient out of bed is one that I presume we will be arguing about for a good many years to come. I believe that we have not much more than scratched the surface of scientific investigation on that point. In recent issue of the *Journal of the American Medical Association*, Blumgart and his associates in an article on cardiac infarction have something of an approach to scientific investigation of that problem. He has attempted to divide coronary artery disease in three ways: 1) those who have angina, (2) those who have an actual closure of a coronary vesses without infarction, and (3) those who have an infarction on the basis of fever and leucocytosis, as well as persistent electrocardiographic findings in addition to pain. On this basis, it seems to me that one has something of a guide to the severity of the condition and can be selective in his instruction to the patient in the matter of getting out of bed. My experience has led me to believe that we are not justified in making a diagnosis of cardiac infarction, and arbitrarily saying that the patient should stay in bed four to six weeks. I believe that we enhance the occurrence of thrombosis by too long rest in bed. We have allowed patients to get out of bed as soon as we saw that the sedimentation rate had taken a definite drop—not necessarily all the way to normal, but a definite drop in the direction of normal. Of course, the patient's clinical condition otherwise must be good. As you know, many patients are anxious to get out of bed as soon as possible and the amount of activity allowed after they do get out of bed is open to considerable judgment. We start by having them hang their feet over the edge of the bed for a few minutes. The following day they are allowed to sit out on a chair for fifteen minutes; and if they do well with this procedure, we gradually increase the time up and the activity. I have never seen any trouble come from this procedure.

Returning to dicoumarol again, if any surgery becomes necessary, such as tying veins when venous thrombosis occurs in the legs, then dicoumarol should be stopped and vitamin K administered.

Perhaps, somewhat off the subject is the question as to the relationship of gallbladder disease to coronary artery disease. Diagnostically, the two conditions can often be very confusing. And, again, when there is infection in the gallbladder, it certainly can aggravate the heart disease—whatever it is. Whether there is any other relationship I do not know.

Another question is the role of heredity in the etiology of coronary artery disease. Heredity is probably the most important single factor in the cause of coronary disease. I cannot quote statistics on this point; but one is constantly impressed with the frequent occurrence of coronary disease in some families. I know of a family in which there were three brothers, a father, an uncle, and a grandfather all afflicted with coronary disease, which manifested itself symptomatically from 40 to 45 years of age in all of them.

INTENSIVE THERAPY OF SYPHILIS*

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The intensive treatment of syphilis as at present understood refers to the proper use of penicillin. The antibiotic therapy of this disease, though scarcely five years have elapsed since its application, has already, apparently justifiably, largely replaced metal chemotherapy. We must, nonetheless, face the fact that the application of the antibiotics to the treatment of syphilis is still in the incipient stage. Time-dose intervals and total dosages are incompletely worked out. Therapeutic results have been reasonably studied for certain stages of the disease only. New preparations are constantly being introduced in an effort to overcome the objections to their predecessors. It is reasonable to suppose that the ideal antibiotic has not yet been found in the treatment of syphilis, but still remains hidden among the numbers of new preparations or substitution products yet to be studied.

In the brief period since its introduction we have seen penicillin used in treatment, modified from a rather crude, impure, unstable amorphous preparation, to various salts (sodium, potassium, calcium) of relatively pure and stable crystalline fractions (G, F, K, X) and more recently have witnessed the introduction of another most valuable substitution product, procaine penicillin. The original aqueous preparations which were absorbed and eliminated or destroyed in the body in a matter of two or three hours have been modified or placed in vehicles to delay their action to the point where twenty-four hour blood levels are easily maintained. With some products such as procaine penicillin to which aluminum monostearate has been added effective and reasonably uniform blood levels have been demonstrated for two to three days. There has been insufficient time since their introduction to properly evaluate most of the delayed action penicillins in the treatment of syphilis. Their use, therefore, must be largely empiric based upon comparison with the first introduced and more thoroughly tried, but rapidly eliminated aqueous preparations.

*Read before the Medical Society of Delaware, Rehoboth, September 15, 1948.

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GENERAL PRINCIPLES IN THE PENICILLIN THERAPY OF SYPHILIS

When to Treat

In this situation it is well to dwell for a few moments on general principles applicable to the field of syphilis therapy as a whole before discussing specific detail of current treatment courses for various stages of syphilis. In the first place, it is, generally speaking, undesirable to treat patients for syphilis unless we are absolutely certain they have the disease. The relative ease of giving penicillin, the short course of treatment, its comparative innocuousness, the general excellence of the results obtained, leave the temptation strong to treat suspicious genital lesions without darkfield examination; to treat positive blood tests without adequate study or confirmation. To inflict a diagnosis of syphilis on any patient has serious medical imports. The protean nature of the disease and its manifest tendency to relapse make its consideration essential in almost every medical problem which arises after a patient has once been diagnosed as having syphilis. It is unfair both to the patient and the physician to induce this situation without careful study and adequate confirmation. The more the question of the non-specific or biologic false positive blood test for syphilis is studied the more it is realized that improper medical evaluation in the past has resulted in the treatment of many non-syphilities for syphilis.

Penicillin therapy, through its very rapid action in the cure of most cases of *infectious* syphilis has suggested one minor exception to the above more or less firmly established rule. With metal chemotherapy as previously employed cure of syphilis was sufficiently slow, a matter of months as a minimum, that some temporary immunity at least, was induced and immediate reinfection was virtually unknown. Today, when penicillin is used to treat recently acquired syphilis the cure is so rapid that little or no immunity is induced and the patient is susceptible, on suitable exposure, to acquiring the disease again after a lapse of a few days or weeks.

Epidemiology to trace sources of infectious syphilis and those who may have been exposed becomes of increasing importance and repeated reinfection of marital partners has become sufficiently common to result in the introduction of the term "ping pong syphilis" by Schoch. Schamberg and Steiger have shown that such cycles of reinfection can be broken when both sex partners are treated simultaneously and Schoch has more recently suggested, on the basis of detailed observations of more than one hundred cases, that immediate treatment following assured exposure to infectious syphilis before the appearance of symptoms will usually prevent the development of the disease. When concerned with individuals who have definitely been exposed to the open lesions of infectious syphilis immediate intensive therapy may be justified.

Treat by Intramuscular Injection

Penicillin in the treatment of syphilis should be given by intramuscular injection. Intravenous injection of aqueous preparations are less effective than intramuscular. Intrathecal use of penicillin in central nervous system involvement is unnecessary since penicillin readily permeates the body membranes. Use of penicillin by ingestion or inhalation is ill advised in the treatment of syphilis because of the uncertainty of absorption and the importance of obtaining adequate dosage in the treatment of a disease potentially as serious as syphilis. A limited trial of penicillin by mouth in the treatment of infantile congenital syphilis at the University of Pennsylvania gave responses sufficiently inferior to the injection method to result in its abandonment.

Maintain Therapeutically Effective Levels for the Entire Course of Treatment

The original penicillin therapy of syphilis consisted in maintaining adequate blood and tissue levels for a period of eight days. Since then many modifications have been introduced including intermittent treatment on a once, twice or three times a week injection schedule which, with the preparations used, is insufficient to maintain continuous blood or tissue levels. In the present state of our knowledge such intermittent methods cannot be recommended, although apparent cure of some patients has resulted from their use. Satisfactory continuous therapeutic levels for the treatment of syphilis are obtained by giving intramuscular injection of the aqueous penicillin 40,000 to 50,000 oxford units every two to three hours around the clock; or by 600,000 oxford units of one of the delayed action penicillins intramuscularly once every 24 hours. It has been shown that penicillin even in large dosage for one or two days does little to affect the course of syphilis. A continuous therapeutic level for from three to five days favorably affects a considerable number of cases. Six to ten days, or in the more severe cases such as central nervous system syphilis fifteen days of continuous penicillin treatment are most apt to produce the desired result. Since little is to be gained and much is to be lost by too small dosage given over too short a period of time, it is best to err on the side of overdosage rather than underdosage. Treatment courses of not less than eight to ten days are accordingly recommended which will result in total penicillin dosages of at least 4.0 to 6.0 million oxford units.

General Considerations As to Cure Rate, Medical Post Treatment Follow-Up and Retreatment

In all patients with syphilis beyond the florid eruptive early stage a spinal fluid examination prior to giving penicillin is indicated. Involvement of the central nervous system, in order to maintain adequate levels in the brain and spinal tissues, requires maximal therapy, usually 10.0 million oxford units over a period of 15 days and a closer medical follow-up, so that this situation should be appraised in advance of therapy.

The best results in the penicillin therapy of syphilis are in the prevention of congenital syphilis where treatment of the mother prenatally will give almost 100 percent non-syphilitic infants. Results in other stages of the disease vary from 70 to 90 percent satisfactory. The appreciable number of treatment failures makes post treatment medical follow-up highly desirable and in most

instances a requisite. With all cases of early syphilis and with pregnant women the follow-up visits should be at monthly intervals at least and should include where possible quantitative titered serologic tests.

Blood serologic response following penicillin therapy of syphilis is not immediate and in general depends upon the duration of the disease at the commencement of treatment. With a recently acquired infection a negative blood test in four to ten months is the rule though an appreciable number of cases respond after more than one year. Provided the quantitative test is progressing to negativity or maintains a relatively low titer the patient need not be considered a treatment failure.

Infectious relapse, serologic relapse or progression in the nervous system (positive spinal fluid) most commonly occurs from three months to one year after treatment and observation of the patient must be most active during this period. Since the blood test may become completely negative and revert to positive after a period of one or more months, obtaining a negative blood test is no reason for immediately discontinuing post treatment observation or discharging the patient as cured.

Where relapse in one form or another or progression occur, one of two forms of handling, in general, is in order. The first procedure would be to retreat with a much larger dose (usually double the initial dose) of penicillin given over a somewhat longer period. The individual dose as well as the total dose should be increased. The rationale behind this comes from the fact, as has been shown experimentally, that some patients fail readily to absorb or to utilize the penicillin given and require much larger doses to obtain detectible blood levels. It has not been found practical to do blood penicillin levels on all patients treated. It has accordingly been recommended empirically that larger doses be given in retreating the cases failing to respond on the chance that the initial dose has been too small. The second mode of approach to the treatment failure case will consist in using supplemental chemotherapy or other treatment (for example fever therapy for central nervous system syphilis or for interstitial keratitis). With the initial treatment of the average case it is not recommended that arsenic or bismuth preparations be used to supplement penicillin therapy. Their ability to enhance the cure rate is slight if any, whereas they greatly increase the possibility of toxicity from treatment. Heavy metal therapy, in particular an insoluble bismuth preparation, is sometimes used following the penicillin course. Such procedure may be necessary to keep the patient under medical observation for the required period of time, since patients will frequently see no reason for returning and drift from medical care if treatment is not given. When to use supplementary treatment under such circumstances, however, is a matter for individual decision.

With this much general comment, I will next briefly discuss the application of penicillin therapy specifically to the various stages of the disease. In this connection it is well to point out that excellent summaries of the penicillin treatment of syphilis as of December 1947 appear in the March 27, 1948 issue of the Journal of the American Medical Association and in the June 1948 issue of the Journal of Venereal Disease Information. Although other preparations of penicillin have increased our therapeutic armamentarium since this information has appeared very little additional has been contributed to our actual knowledge of the penicillin therapy of syphilis.

Symptomatic Early Syphilis

Total dosage of penicillin should be between 4.0 and 6.0 million oxford units over a period of 8 to 10 days. Aqueous preparations which will require hospitalization because of the frequency of administration should be given in amount of 40,000 to 50,000 oxford units intramuscularly every two or three hours for a total of 100 injections.

If one of the delayed action penicillins is used ambulatory treatment is possible and 600,000 units intramuscularly one daily for a total of ten injections should be employed. In the one injection a day technique it is preferable that the treatment be given at the same time each day and that it be administer-

ed close to bedtime, that is for the average patient in the late afternoon or early evening. This makes it so that the maximum concentration is contained in the buttock during the period of rest and so that the person is active and massaging the hip through motion during the period when the concentration in the buttock is smallest. We are often confronted also with the necessity of omitting one or more injections from the course as for example on Sunday or sometimes on both Saturday and Sunday. If such is the case it is probably best to have interruptions close to the end of the course than at the beginning. Thus, if the treatment is to be interrupted for Saturday or Sunday or for both days it would be preferable to have the treatment course start on Monday. If the patient reports with infectious lesions during the week it would be possible to give one or two injections of an arsenical (phenarsine derivative) to render the lesions relatively spirochete free preparatory to commencing penicillin therapy. This method of approach would make it possible to commence the intensive penicillin therapy on any desired day and at the same time meet the public health obligation.

There can be no doubt that uniform hospitalization of patients with open infectious lesions is desirable, and that in the present state of our knowledge an uninterrupted penicillin course is preferable.

Arsenical, bismuth or fever to supplement the initial course of penicillin have no advantage over penicillin alone as has been remarked upon above. Once a patient has relapsed or has failed to respond to initial therapy, the chances that he will be cured by subsequent treatment are greatly reduced. In such instances in addition to repetition of the penicillin course arsenic and bismuth may be used. The recommendation of the Syphilis Study Section of the National Institute of Health is for "600 mg oxophenarsine hydrochloride given every other day in 10 intravenous injections of 60 mg over a total of 19 days and 200 mg of bismuth subsalicylate in oil given every five to seven days in 10 intramuscular injections of 200 mg each over a total period of fifty to seventy days."

Latent Syphilis

The use of penicillin in the treatment of latent syphilis must of necessity be based upon our knowledge of its use in other stages of the disease. The only way that the value of therapy can be determined in the treatment of latent syphilis is through prolonged observation to detect progression. Penicillin seems to be no more effective in reversing the blood serologic test in patients with latent syphilis than are other types of therapy. The shorter the duration of the disease before treatment is commenced the greater the likelihood of a satisfactory serologic response, but in general fully fifty percent of cases of latent syphilis will still be seropositive two to three years after the completion of penicillin therapy.

If penicillin is used in the treatment of such patients it must be given in arbitrary amount and the individual then observed every six months to one year for an indefinite period for evidence of progression of his disease. In the absence of evidence of progression there is no indication for retreatment. The penicillin dosage usually employed is the same as for the treatment of symptomatic early syphilis on the assumption that if this amount of treatment will cure patients with early syphilis it should also cure patients with latent syphilis. It will require many years to be certain that this assumption is justified.

Syphilitic Pregnant Woman

Penicillin therapy is the treatment of choice of the pregnant syphilitic woman to prevent congenital syphilis. No adjunct metal chemotherapy with arsenic or bismuth is necessary.

Results approaching 100 percent in the protection of the foetus may be obtained by maintaining adequate penicillin blood and tissue levels continuously for from seven to eight days.

This may be effectively accomplished by giving:

(1) 40,000 or more oxford units Sodium penicillin (crystalline G) in aqueous solution intramuscularly every two to three hours over a period of eight days, totalling not less than

2.4 million oxford units. (requires hospitalization).

(2) 600,000 units penicillin in oil wax once daily for eight days. Total dose 4.8 million units.

(3) Presumably similar dosage of procaine penicillin once daily, once every other day or even longer intervals, provided adequate blood and tissue levels are maintained to insure penetration of the placenta.

It should be noted that amounts of penicillin insufficient to cure the disease in the mother will nonetheless usually prevent infection of the foetus. The dosage above given is minimal. In general it is best to treat the pregnant woman with the amount of penicillin required for the stage of the disease presented irrespective of pregnancy.

This treatment may be used in the pregnant woman *in any stage of syphilis* in which penicillin is applicable. *A single course of treatment at any time in the pregnancy* is usually all that is required to protect the foetus. If treatment is given prior to the twentieth week of the pregnancy the foetus will probably not have been infected and the transmission of the disease will have been prevented in the true sense. If treatment is given in the latter months of the pregnancy the foetus may already have been infected under which circumstances it is particularly necessary to maintain high 24 hour blood levels of penicillin to insure satisfactory permeation of the placenta. This can be best accomplished with our present knowledge by using larger dosage (4.0 million units and up total dose) of aqueous sodium penicillin given at frequent (2-3 hour) intervals.

Medical follow-up (1) *Of Mother*: Following the penicillin course the mother should have a physical inspection for syphilitic lesions and a quantitative titered blood serologic test for syphilis once monthly until term. Retreatment just before delivery should be resorted to for (a) development of infectious lesions of syphilis, (b) an appreciable confirmed increase in the titer of the blood serologic test, (c) a high sustained titer of the serologic test. Medical follow-up of the mother after delivery for at least one year is also important to insure cure of her disease.

(2) *Of Infant*: A blood serologic test should always be taken on the mother at the time of delivery. If this is positive a positive test on the infant during the neonatal period is not considered of diagnostic significance unless there is collateral evidence of syphilis. A blood test should be taken on all infants of syphilitic mothers on the nursery and at the age of one month, two months and six months as a minimum. A persistently positive test of high titer beyond the first month is usually indicative of congenital syphilis, and beyond the second month is almost always diagnostic of congenital syphilis. A negative blood serologic test at six months of age will adequately rule out congenital syphilis. Properly interpreted roentgenograms of the long bones of the infant between the ages of one and eight weeks are important collateral diagnostic aids. Skin lesions (other than macules) of infantile congenital syphilis are almost always darkfield positive during this period.

Infantile Congenital Syphilis

Penicillin therapy is the treatment of choice in infantile congenital syphilis. No adjunct metal chemotherapy with arsenic or bismuth is necessary.

Results approaching 100 percent satisfactory may be obtained in surviving infants where treatment is commenced before the third month of life and are about 70 percent satisfactory where treatment is commenced between three months and two years. Treatment failures seldom result in infectious relapse but usually in seroresistance.

(1) Young and debilitated infants should be hospitalized and given expert supportive pediatric care. Specific therapy should be commenced immediately upon establishing the diagnosis of syphilis. Aqeuous sodium penicillin given intramuscularly should be employed in total dose of not less than 100,000 units per pound of body weight given in 120 divided doses every three hours over a period of 15 days.

(2) Older infants not debilitated may be given one of the delayed action penicillins on an ambulatory basis in dosage of 150,000 to 300,000 units daily over a period of 10 to 15 days.

Medical Follow-Up

A physical inspection and blood serologic

test should be taken once monthly for one year following completion of treatment.

A spinal fluid examination should be performed on all cases between 6 months and one year after therapy.

A persistently positive blood serologic test after one year will probably require retreatment. A positive spinal fluid will require individualized, specialized attention.

Active Interstitial Keratitis

Such cases should be hospitalized for best results and given fever therapy under expert supervision in addition to maximum penicillin dosage (total 6.0 to 10.0 million oxford units) over a period of 15 days. This is one stage of syphilis where results though often good, must have a guardedly favorable prognosis, since relapse and progression are common in as high as 30 percent of cases. The best treatment of interstitial keratitis is preventative which may usually be accomplished by detection and treatment of infantile congenital syphilis.

Central Nervous System Syphilis

The treatment of central nervous system involvement from syphilis must be largely individualized and it is difficult to talk of it in such a short presentation, in terms of anything other than broad general principles. When syphilis is of long standing as is usually the case when central nervous system involvement is detected arrest of the disease does not always result in cure of the patient. Regeneration of nervous tissue cannot be expected and where vascular damage has occurred progression of the disease may result in spite of and at times presumably even as a result of treatment.

With these reservations penicillin alone has proved to be a very valuable drug in the treatment of central nervous system syphilis. The blood serologic test is not usually affected by treatment and behaves much in the same manner as with other cases of late syphilis. The spinal fluid response is good, particularly in asymptomatic neurosyphilis and in symptomatic neurosyphilis other than paresis and taboparesis. In these categories about three-fourths in our experience have become normal within a year following treatment. In frank paresis and taboparesis almost two-thirds of the spinal fluids have remained abnormal in some degree after two years of post treatment observation, but the majority have greatly improved and fall in the category of near normal. Definite central nervous system relapses following penicillin therapy have been uncommon in the short periods of observation (two to four years) and in the magnitude of no more than one or two percent.

So far as improvement or arrest of clinical symptoms is concerned penicillin has proved to be equal to or better than other modes of treatment of central nervous system syphilis with the exception of frank paresis. With paresis the use of penicillin alone is slower in producing remission though perhaps not inferior in final results, to chemotherapy or penicillin *plus fever therapy.*

With central nervous system syphilis large dosage of penicillin (in the magnitude of 10 to 20 million oxford units total) should be used over a ten to twenty day period, preferably on a hospitalized patient. Medical follow-up observation including repetition of the spinal fluid study should be done at three to six month intervals and later at yearly intervals almost indefinitely. Retreatment for failure of complete response is frequently resorted to.

Summary

Penicillin is a most effective remedy for the treatment of syphilis and for most stages of the disease is treatment of choice. Satisfactory treatment courses have been evolved and are given for symptomatic early syphilis, syphilis and pregnancy, and infantile congenital syphilis. Most of the late stages of the disease will require considerably longer periods of observation before definite conclusions as to effective therapy may be reached, although the preliminary results with most types of neurosyphilis have been good. New preparations are constantly being introduced most of which have not been evaluated in the treatment of syphilis. Aqueous solutions of penicillin have been most thoroughly tried in the treatment of syphilis but it is generally assumed that delayed action penicillins are just as effective provided they produce detectible twenty-four hour blood levels. As new antibiotics are developed the therapy of syphilis will most likely be still further modified.

+ Editorials +

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The 1949 Meeting

The 160th Annual Session of the Medical Society of Delaware was held at the Hotel Du Pont, Wilmington, on October 10-12, 1949, President M. A. Tarumianz of Farnhurst, presiding.

The meeting of the House of Delegates was notable for the despatch with which its transactions were handled, many of the reports involving routine statistics being read by title. The main business of the evening was the reading and tentative adoption of a new set of By-Laws. As amended, these will be sent to each of the county societies after October 27th, in order to give the necessary two months' notice as required by the old By-Laws. Each society will then formally approve the new By-Laws, and so notify the Secretary, after which they will be declared in effect. The transactions will be printed in the December issue of The Journal, and the new By-Laws in a separate booklet.

The scientific meetings proceeded exactly as printed in the September Journal, every scheduled essaying being present. These papers were of a high order, and were well received and adequately discussed.

The elections for the year 1950 resulted as follows:

President, Carl B. Scull ..... Dover
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The Woman's Auxiliary met at the Delaware Academy of Medicine and the Hotel Rodney, under the Presidency of Mrs. Roger Murray, of Wilmington. A business session on October 11th was followed by their own luncheon, attended by 68 members and guests. On October 12th, at another business session the following officers for 1949-50 were elected and installed:

President, Mrs. J. Leland Fox ..... Seaford
President-elect, Mrs. Jos. M. Messick, Wilmington
Recording Sec'y, Mrs. Andrew M. Gehret, Wilm.
Corresponding Sec'y, Mrs. Chas. M. Moyer, Laurel
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The social events were particularly pleasant. Preceeding the meeting of the House of Delegates President Tarumianz gave a dinner for the officers and chairmen of committees. Following the House there was a social hour for all the members present. The luncheon by the New Castle County Society on October 11 was attended by 100 guests, and that given by the State Society on October 12 was attended by 175 guests. The main social event was the reception and dinner on October 11, which was attended by 130 subscribers, and was addressed most entertainly by Edward R. Rosse, humorist and philosopher of Philadelphia.

The technical exhibits again set a new record for number and income, there being 27 exhibitors occupying 29 booths. With the expansion of the Society's activities and the increasing costs thereof the Society is becoming more and more dependent upon the financial success of its technical exhibit to make its convention expenses balance. Our exhibitors this year seemed pleased with the arrangements made for them, and several stated they would be with us again next year at Dover.

The registration was as follows:

House of Delegates	41
Scientific Meetings	106
Members	147
Guests, Visitors, etc.	38
Residents, Internes, etc.	20
Exhibitors	52
Medical Society	257
Woman's Auxiliary	68
Total	325

The membership registration, 147 of a total of 291, was 50.5%, which we believe is well above the national average for a state medical convention.

So passes into history the 1949 Session. Now let us turn our faces towards Dover and make the 1950 Session an even better one.

THE AMA COUNTS 16

September 8, 1949

Dr. W. Edwin Bird, M. D.
822 North American Building
Wilmington, Delaware
Dear Dr. Bird:

I am more than a little surprised that there has been some confusion about the exact meaning of our editorial, "The AMA Counts 16," which appeared in the *Morning News* of Sept. 1. It seemed to me that we had made it quite clear that we felt that the American Medical Association had produced 16 impressive arguments to support its charge that President Truman's national medical insurance plan would come close to setting up a government dictatorship over the medical profession. However, since you say there has been confusion, we must have fallen short somewhere since the first duty of an editorial writer is to make sure that his point of view is clear and understandable.

The editorial was intended to congratulate the AMA on producing concrete evidence to support its accusations that the Truman health program would lead to dictatorship. When we said that "It has compiled a list of 16 points in support of its position" we were referring to AMA's position, and I don't think that there can be much doubt what that is. After listing the 16 points we said: "It is no overstatement that the powers listed would be vast, possibly dangerous," and added "The AMA, in short, has managed to make out a strong case." Perhaps we should have written "a strong case against President Truman's national medical insurance plan" but this hardly seemed necessary in view of what we had already said and the long and strenuous campaign which the AMA has waged against this program.

At any rate, I hope that this will clear up any possible misunderstanding about the position of the *Morning News* and the intent of the editorial in question. You have our permission, of course, to reprint the editorial in THE JOURNAL together with this letter.

With best regards,

Sincerely yours,
Charles L. Reese, Jr.
Executive Editor

ge

THE COMMON COLD

"Acetylsalicylic acid (aspirin) does not have any influence on the infectious process of the common cold. Symptomatic relief of headache, fever and muscle pain is, nevertheless, of value as long as the drug does not disguise the need for more vigorous treatment. A false sense of improvement may occasionally occur, thereby permitting the patient to resume activity too soon. Numerous cough mixtures to which laymen resort without the advice of a physician are of doubtful value. Expectorants or respiratory sedatives are best prescribed by the physician, as the preparation of the cough mixture should be governed by the type of cough and the age of the patient.

"From time to time claims are advanced for special diets for either the prevention or the cure of colds. The dietary measures most frequently recommended for the prevention of colds include a high protein diet, a diet low in carbohydrates and large quantities of citrus foods, presumably to establish 'alkalinization.' None of these theories is supported by carefully controlled studies. The supplying of extra vitamins and other food elements to the person who does not show signs of deficiency disease does not protect him against colds. Procedures which have as their objective the conditioning of the body to sudden changes in external temperature of the skin, such as cold and hot shower baths, do not lower the incidence of the common cold. The scientific evidence against the value of oral cold vaccines is overwhelming.

"The treatment of the common cold consists mainly in the relief of symptoms as they arise. During the earliest stages of the common cold the prime objective is to supply moisture by means of steam inhalations to the stricken upper respiratory passages. Alcohol has been utilized for generations to abort impending colds or to treat them. In reasonable doses it causes peripheral vasodilatation and reestablishes circulation in chilled cutaneous and mucosal surfaces.

"Little attention need be paid to fluids in the average uncomplicated cold; it is probably best to let thirst to a great extent determine the fluid intake. Cathartics and laxatives, long employed as home remedies for colds, do not have particular value; their excessive use may lead to dehydration. Rest in bed, especially if fever is present, diminishes the severity of the common cold, limits its spread to others and reduces the frequency of complications. It has stood the rigid test of time as a most sane and effective measure."

AMA News.

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STATEMENT OF OWNERSHIP, MANAGEMENT, CIRCULATION, ETC.

Required by the Act of Congress of August 24, 1912, and March 3, 1933, of The Delaware State Medical Journal, Published monthly at Wilmington, Delaware, for October 1st, 1949

STATE OF DELAWARE } SS
COUNTY OF NEW CASTLE }

Before me, a Notary Public in and for the State and county aforesaid, personally appeared M. A. Tarumianz, M. D., who, having been duly sworn according to law, deposes and says that he is the Managing Editor of the Delaware State Medical Journal and that the following is, to the best of his knowledge and belief, a true statement of the ownership, management (and if a daily paper, the circulation) etc., of the aforesaid publication for the date shown in the above caption, required by the Act of August 24, 1912 as amended by the Act of March 3, 1933, embodied in section 537, Postal Laws and Regulations, printed on the reverse of this form, to wit:

1. That the names and addresses of the publisher, editor, managing editor, and associate editor are:

Name of— Post Office Address

Publisher—Star Publishing Co., 309 Shipley St., Wilmington, Del.

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2. That the owner is: (if owned by a corporation, its name and address must be stated and also immediately thereunder the names and addresses of stockholders owning or holding one per cent or more of total amount of stock. If not owned by a corporation, the names and addresses of the individual owners must be given. If owned by a firm, company, or other unincorporated concern, its name and address, as well as those of each individual member, must be given.)

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4. That the two paragraphs next above, giving the names of the owners, stockholders and security holders, if any, contain not only the list of stockholders and security holders as they appear upon the books of the company but also, in cases where the stockholder or security holder appears upon the books of the company as trustee or in any other fiduciary relation, the name of the person or corporation for whom such trustee is acting, is given; also that the said two paragraphs contain statements embracing affiant's full knowledge and belief as to the circumstances and conditions under which stockholders and security holders who do not appear upon the books of the company as trustees, hold stock and securities in a capacity other than that of a bona fide owner; and this affiant has no reason to believe that any other person, association, or corporation has any interest direct or indirect in the said stock, bonds, or other securities than as so stated by him.

5. That the average number of copies of each issue of this publication sold or distributed, through the mails or otherwise, to paid subscribers during the twelve months preceding the date shown above is ——— (This information is required from daily publications only.)

M. A. TARUMIANZ, M. D.
(Signature of Business Manager)

Sworn to and subscribed before me this 9th day of September, 1949.

KENNETH GOODE
Notary Public
(My commission expires Oct. 5, 1950)

A roentgenographically normal chest in a person over 40 does not eliminate the possibility of pulmonary tuberculosis developing in the future. Incipient pulmonary tuberculosis in persons over 40 may be much more common than is generally supposed. Aaron D. Chaves, M.D., Am. Rev. Tuberc., May, 1949.

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